

# ROYAUME DE BELGIQUE

MINISTÈRE DES AFFAIRES ÉCONOMIQUES  
ADMINISTRATION DE LA POLITIQUE COMMERCIALE



REC'D 20 AUG 2004  
WIPO PCT

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Il est certifié que les annexes à la présente sont la copie fidèle de documents que détient l'Office de la Propriété Industrielle.

Bruxelles, le 24. -6 - 2004

## PRIORITY DOCUMENT

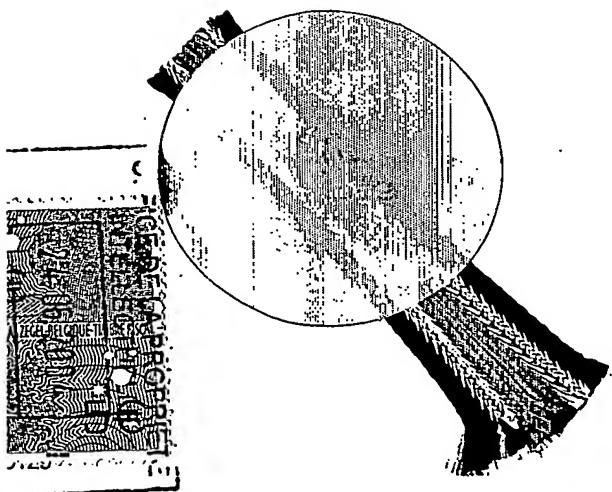
SUBMITTED OR TRANSMITTED IN  
COMPLIANCE WITH RULE 17.1(a) OR (b)

Pour le Conseiller de l'Office  
de la Propriété industrielle

Le fonctionnaire délégué,

A handwritten signature in black ink, appearing to read "Bailleux".

BAILLEUX G.  
Conseiller adjoint



PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

|   |   |  |   |  |               |  |                 |  |  |
|---|---|--|---|--|---------------|--|-----------------|--|--|
| For receiving Office use only<br>PCT/BE03/00112   |   |  |   |  |               |  |                 |  |  |
| International Application No.<br><b>(26 -06- 2003)</b>  |   |  |   |  |               |  |                 |  |  |
| 26 JUIN 2003<br>International Filing Date   |   |  |   |  |               |  |                 |  |  |
| <b>RO/BE - INTERNATIONAL APPLICATION</b>  |   |  |   |  |               |  |                 |  |  |
| Name of receiving Office and "PCT International Application"  |   |  |   |  |               |  |                 |  |  |
| Applicant's or agent's file reference<br>(if desired) (12 characters maximum) ORPC 134.783 JV   |   |  |   |  |               |  |                 |  |  |
| <b>Box No. I TITLE OF INVENTION</b><br>Livestock products with an increased PPAR/RXR heterodimer activator level  |   |  |   |  |               |  |                 |  |  |
| <b>Box No. II APPLICANT</b> <div style="display: flex; justify-content: space-between;"> <input type="checkbox"/> This person is also inventor         </div> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 60%;">Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)<br/><br/>INVE Technologies NV<br/>Hoogveld 93<br/>B-9200 Dendermonde</td> <td style="width: 40%;">Telephone No.</td> </tr> <tr> <td></td> <td>Facsimile No.</td> </tr> <tr> <td></td> <td>Teleprinter No.</td> </tr> <tr> <td></td> <td>Applicant's registration No. with the Office</td> </tr> </table>          |   | Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)<br><br>INVE Technologies NV<br>Hoogveld 93<br>B-9200 Dendermonde | Telephone No.   |  | Facsimile No. |  | Teleprinter No. |  | Applicant's registration No. with the Office |
| Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)<br><br>INVE Technologies NV<br>Hoogveld 93<br>B-9200 Dendermonde  | Telephone No.   |  |   |  |               |  |                 |  |  |
|   | Facsimile No.   |  |   |  |               |  |                 |  |  |
|   | Teleprinter No.   |  |   |  |               |  |                 |  |  |
|   | Applicant's registration No. with the Office  |  |   |  |               |  |                 |  |  |
| State (that is, country) of nationality:<br>BE  |   |  |   |  |               |  |                 |  |  |
| State (that is, country) of residence:<br>BE  |   |  |   |  |               |  |                 |  |  |
| This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input checked="" type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box   |   |  |   |  |               |  |                 |  |  |
| <b>Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)</b> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 60%;">Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)<br/><br/>DE KEYSER Luc<br/>Stationsstraat 40<br/>B-9470 Denderleeuw</td> <td style="width: 40%;">This person is:<br/><br/><input type="checkbox"/> applicant only<br/><input checked="" type="checkbox"/> applicant and inventor<br/><input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)<br/><br/>Applicant's registration No. with the Office</td> </tr> </table> |   | Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)<br><br>DE KEYSER Luc<br>Stationsstraat 40<br>B-9470 Denderleeuw  | This person is:<br><br><input type="checkbox"/> applicant only<br><input checked="" type="checkbox"/> applicant and inventor<br><input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)<br><br>Applicant's registration No. with the Office |  |               |  |                 |  |  |
| Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)<br><br>DE KEYSER Luc<br>Stationsstraat 40<br>B-9470 Denderleeuw   | This person is:<br><br><input type="checkbox"/> applicant only<br><input checked="" type="checkbox"/> applicant and inventor<br><input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)<br><br>Applicant's registration No. with the Office |  |   |  |               |  |                 |  |  |
| State (that is, country) of nationality:<br>BE  |   |  |   |  |               |  |                 |  |  |
| State (that is, country) of residence:<br>BE  |   |  |   |  |               |  |                 |  |  |
| This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box   |   |  |   |  |               |  |                 |  |  |
| <input type="checkbox"/> Further applicants and/or (further) inventors are indicated on a continuation sheet.   |   |  |   |  |               |  |                 |  |  |
| <b>Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE</b>   |   |  |   |  |               |  |                 |  |  |
| The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: <input checked="" type="checkbox"/> agent <input type="checkbox"/> common representative   |   |  |   |  |               |  |                 |  |  |
| Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)<br><br>VAN REET Joseph<br>Gevers & Vander Haeghen<br>Holidaystraat 5<br>B-1831 Diegem<br>Belgium   |   |  |   |  |               |  |                 |  |  |
| Telephone No.<br>32 2 535 99 11   |   |  |   |  |               |  |                 |  |  |
| Facsimile No.<br>32 2 535 99 00   |   |  |   |  |               |  |                 |  |  |
| Teleprinter No.   |   |  |   |  |               |  |                 |  |  |
| Agent's registration No. with the Office<br>0517  |   |  |   |  |               |  |                 |  |  |
| <input type="checkbox"/> Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.  |   |  |   |  |               |  |                 |  |  |

Sheet No. ...2...

## Box No. V DESIGNATION OF STATES

Mark the applicable check-boxes below; at least one must be marked.

The following designations are hereby made under Rule 4.9(a):

## Regional Patent

- AP ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, MZ Mozambique, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZM Zambia, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT (if other kind of protection or treatment desired, specify on dotted line) .....
- EA Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT .....
- EP European Patent: AT Austria, BE Belgium, BG Bulgaria, CH & LI Switzerland and Liechtenstein, CY Cyprus, CZ Czech Republic, DE Germany, DK Denmark, EE Estonia, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, SI Slovenia, SK Slovakia, TR Turkey, and any other State which is a Contracting State of the European Patent Convention and of the PCT .....
- OA OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GQ Equatorial Guinea, GW Guiné-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line) .....

## National Patent (if other kind of protection or treatment desired, specify on dotted line):

- |   |  |   |
|---|--|---|
| <input checked="" type="checkbox"/> AE United Arab Emirates .....               | <input checked="" type="checkbox"/> GM Gambia .....                                    | <input checked="" type="checkbox"/> NZ New Zealand .....                      |
| <input checked="" type="checkbox"/> AG Antigua and Barbuda .....                | <input checked="" type="checkbox"/> HR Croatia .....                                   | <input checked="" type="checkbox"/> OM Oman .....                             |
| <input checked="" type="checkbox"/> AL Albania .....                            | <input checked="" type="checkbox"/> HU Hungary .....                                   | <input checked="" type="checkbox"/> PH Philippines .....                      |
| <input checked="" type="checkbox"/> AM Armenia .....                            | <input checked="" type="checkbox"/> ID Indonesia .....                                 | <input checked="" type="checkbox"/> PL Poland .....                           |
| <input checked="" type="checkbox"/> AT Austria .+ utility model .....           | <input checked="" type="checkbox"/> IL Israel .....                                    | <input checked="" type="checkbox"/> PT Portugal .....                         |
| <input checked="" type="checkbox"/> AU Australia .....                          | <input checked="" type="checkbox"/> IN India .....                                     | <input checked="" type="checkbox"/> RO Romania .....                          |
| <input checked="" type="checkbox"/> AZ Azerbaijan .....                         | <input checked="" type="checkbox"/> IS Iceland .....                                   | <input checked="" type="checkbox"/> RU Russian Federation .....               |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina .....             | <input checked="" type="checkbox"/> JP Japan .....                                     |   |
| <input checked="" type="checkbox"/> BB Barbados .....                           | <input checked="" type="checkbox"/> KE Kenya .....                                     | <input checked="" type="checkbox"/> SC Seychelles .....                       |
| <input checked="" type="checkbox"/> BG Bulgaria .....                           | <input checked="" type="checkbox"/> KG Kyrgyzstan .....                                | <input checked="" type="checkbox"/> SD Sudan .....                            |
| <input checked="" type="checkbox"/> BR Brazil .....                             | <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea .....     | <input checked="" type="checkbox"/> SE Sweden .....                           |
| <input checked="" type="checkbox"/> BY Belarus .....                            | <input checked="" type="checkbox"/> KR Republic of Korea .....                         | <input checked="" type="checkbox"/> SG Singapore .....                        |
| <input checked="" type="checkbox"/> BZ Belize .....                             | <input checked="" type="checkbox"/> KZ Kazakhstan .....                                | <input checked="" type="checkbox"/> SK Slovakia .+ utility model .....        |
| <input checked="" type="checkbox"/> CA Canada .....                             | <input checked="" type="checkbox"/> LC Saint Lucia .....                               | <input checked="" type="checkbox"/> SL Sierra Leone .....                     |
| <input checked="" type="checkbox"/> CH & LI Switzerland and Liechtenstein ..... | <input checked="" type="checkbox"/> LK Sri Lanka .....                                 | <input checked="" type="checkbox"/> TJ Tajikistan .....                       |
| <input checked="" type="checkbox"/> CN China .....                              | <input checked="" type="checkbox"/> LR Liberia .....                                   | <input checked="" type="checkbox"/> TM Turkmenistan .....                     |
| <input checked="" type="checkbox"/> CO Colombia .....                           | <input checked="" type="checkbox"/> LS Lesotho .....                                   | <input checked="" type="checkbox"/> TN Tunisia .....                          |
| <input checked="" type="checkbox"/> CR Costa Rica .....                         | <input checked="" type="checkbox"/> LT Lithuania .....                                 | <input checked="" type="checkbox"/> TR Turkey .....                           |
| <input checked="" type="checkbox"/> CU Cuba .....                               | <input checked="" type="checkbox"/> LU Luxembourg .....                                | <input checked="" type="checkbox"/> TT Trinidad and Tobago .....              |
| <input checked="" type="checkbox"/> CZ Czech Republic .+ utility model .....    | <input checked="" type="checkbox"/> LV Latvia .....                                    | <input checked="" type="checkbox"/> TZ United Republic of Tanzania .....      |
| <input checked="" type="checkbox"/> DE Germany .....                            | <input checked="" type="checkbox"/> MA Morocco .....                                   | <input checked="" type="checkbox"/> UA Ukraine .....                          |
| <input checked="" type="checkbox"/> DK Denmark .....                            | <input checked="" type="checkbox"/> MD Republic of Moldova .....                       | <input checked="" type="checkbox"/> UG Uganda .....                           |
| <input checked="" type="checkbox"/> DM Dominica .....                           | <input checked="" type="checkbox"/> MG Madagascar .....                                | <input checked="" type="checkbox"/> US United States of America .....         |
| <input checked="" type="checkbox"/> DZ Algeria .....                            | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia ..... | <input checked="" type="checkbox"/> UZ Uzbekistan .....                       |
| <input checked="" type="checkbox"/> EC Ecuador .....                            | <input checked="" type="checkbox"/> MN Mongolia .....                                  | <input checked="" type="checkbox"/> VC Saint Vincent and the Grenadines ..... |
| <input checked="" type="checkbox"/> EE Estonia .....                            | <input checked="" type="checkbox"/> MW Malawi .....                                    | <input checked="" type="checkbox"/> VN Viet Nam .....                         |
| <input checked="" type="checkbox"/> ES Spain .....                              | <input checked="" type="checkbox"/> MX Mexico .....                                    | <input checked="" type="checkbox"/> YU Yugoslavia .....                       |
| <input checked="" type="checkbox"/> FI Finland .....                            | <input checked="" type="checkbox"/> MZ Mozambique .....                                | <input checked="" type="checkbox"/> ZA South Africa .....                     |
| <input checked="" type="checkbox"/> GB United Kingdom .....                     | <input checked="" type="checkbox"/> NO Norway .....                                    | <input checked="" type="checkbox"/> ZM Zambia .....                           |
| <input checked="" type="checkbox"/> GD Grenada .....                            |  | <input checked="" type="checkbox"/> ZW Zimbabwe .....                         |
| <input checked="" type="checkbox"/> GE Georgia .....                            |  |   |
| <input checked="" type="checkbox"/> GH Ghana .....                              |  |   |

Check-boxes below reserved for designating  
 and any other state which is .....

States which have become party to the PCT after issuance of this sheet:

- NI Nicaragua .....
- /date of the international filing .....
- PG Papua New Guinea .....
- SY Syrian Arab Republic .....

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)

**Supplemental Box**      *If the Supplemental Box is not used, this sheet should not be included in the request.*

1. *If, in any of the Boxes, except Boxes Nos. VIII(i) to (v) for which a special continuation box is provided, the space is insufficient to furnish all the information: in such case, write "Continuation of Box No...." (indicate the number of the Box) and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient, in particular:*
  - (i) *if more than two persons are to be indicated as applicants and/or inventors and no "continuation sheet" is available: in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below;*
  - (ii) *if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;*
  - (iii) *if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;*
  - (iv) *if, in addition to the agent(s) indicated in Box No. IV, there are further agents: in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;*
  - (v) *if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "continuation" or "continuation-in-part": in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;*
  - (vi) *if, in Box No. VI, there are more than five earlier applications whose priority is claimed: in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI.*
2. *If, with regard to the precautionary designation statement contained in Box No. V, the applicant wishes to exclude any State(s) from the scope of that statement: in such case, write "Designation(s) excluded from precautionary designation statement" and indicate the name or two-letter code of each State so excluded.*

#### CONTINUATION OF BOX IV ADDITIONAL AGENTS :

Claeys Pierre, Gevers Florent, Gevers François,  
 Gevers Jacques, Grisar Daniel, Luys Marie-José,  
 Pieraerts Jacques, Quintelier Claude, Rossini -de  
 Taxis du Poët Dominique, Schmitz Yvon, Van Reet  
 Joseph, Vossinkel Philippe

#### Professional address :

Gevers & Vander Haeghen  
 Holidaystraat 5  
 B-1831 Diegem  
 Belgium

Telephone N° : 32 2 535 99 11

Fax N° : 32 2 535 99 00

Sheet No. ...4...

**Box No. VI PRIORITY CLAIM**

The priority of the following earlier application(s) is hereby claimed:

| Filing date<br>of earlier application<br>(day/month/year) | Number<br>of earlier application | Where earlier application is:                        |                        |  |
|---|----------------------------------|--|------------------------|--|
|   |                                  | national application:<br>country or Member<br>of WTO | regional application:* | international application:<br>receiving Office |
| item (1)  |                                  |  |                        |  |
| item (2)  |                                  |  |                        |  |
| item (3)  |                                  |  |                        |  |
| item (4)  |                                  |  |                        |  |
| item (5)  |                                  |  |                        |  |

 Further priority claims are indicated in the Supplemental Box.

The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (*only if the earlier application was filed with the Office which for the purposes of this international application is the receiving Office*) identified above as:

all items     item (1)     item (2)     item (3)     item (4)     item (5)     other, see  
Supplemental Box

\* Where the earlier application is an ARIPO application, indicate at least one country party to the Paris Convention for the Protection of Industrial Property or one Member of the World Trade Organization for which that earlier application was filed (Rule 4.10(b)(ii)): .....

**Box No. VII INTERNATIONAL SEARCHING AUTHORITY**

Choice of International Searching Authority (ISA) (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

ISA / .....

Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):

|                       |        |                              |
|-----------------------|--------|------------------------------|
| Date (day/month/year) | Number | Country (or regional Office) |
|-----------------------|--------|------------------------------|

**Box No. VIII DECLARATIONS**

The following declarations are contained in Boxes Nos. VIII (i) to (v) (mark the applicable check-boxes below and indicate in the right column the number of each type of declaration):

Number of declarations

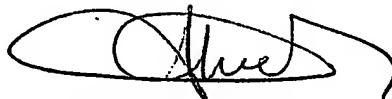
- |   |  |   |
|---|--|---|
| <input type="checkbox"/> Box No. VIII (i)   | Declaration as to the identity of the inventor   | : |
| <input type="checkbox"/> Box No. VIII (ii)  | Declaration as to the applicant's entitlement, as at the international filing date, to apply for and be granted a patent             | : |
| <input type="checkbox"/> Box No. VIII (iii) | Declaration as to the applicant's entitlement, as at the international filing date, to claim the priority of the earlier application | : |
| <input type="checkbox"/> Box No. VIII (iv)  | Declaration of inventorship (only for the purposes of the designation of the United States of America)                               | : |
| <input type="checkbox"/> Box No. VIII (v)   | Declaration as to non-prejudicial disclosures or exceptions to lack of novelty   | : |

## Box No. IX CHECK LIST; LANGUAGE OF FILING

|   |           |                 |
|---|-----------|-----------------|
| This international application contains:  |           | Number of items |
| (a) in paper form, the following number of sheets :   |           |                 |
| request (including declaration sheets)  | : 5       |                 |
| description (excluding sequence listings and/or tables related thereto)   | : 34      |                 |
| claims  | : 8       |                 |
| abstract  | : 1       |                 |
| drawings  |           |                 |
| <b>Sub-total number of sheets</b>   | <b>48</b> |                 |
| sequence listings   |           |                 |
| tables related thereto  |           |                 |
| <i>(for both, actual number of sheets if filed in paper form, whether or not also filed in computer readable form; see (c) below)</i>   |           |                 |
| Total number of sheets  | 48        |                 |
| (b) <input type="checkbox"/> only in computer readable form (Section 801(a)(i))   |           |                 |
| (i) <input type="checkbox"/> sequence listings  |           |                 |
| (ii) <input type="checkbox"/> tables related thereto  |           |                 |
| (c) <input type="checkbox"/> also in computer readable form (Section 801(a)(ii))  |           |                 |
| (i) <input type="checkbox"/> sequence listings  |           |                 |
| (ii) <input type="checkbox"/> tables related thereto  |           |                 |
| Type and number of carriers (diskette, CD-ROM, CD-R or other) on which are contained the  |           |                 |
| <input type="checkbox"/> sequence listings: .....   |           |                 |
| <input type="checkbox"/> tables related thereto: .....  |           |                 |
| <i>(additional copies to be indicated under items 9(ii) and/or 10(ii), in right column)</i>   |           |                 |
| This international application is accompanied by the following item(s) (mark the applicable check-boxes below and indicate in right column the number of each item):  |           |                 |
| 1. <input checked="" type="checkbox"/> fee calculation sheet  |           |                 |
| 2. <input type="checkbox"/> original separate power of attorney   |           |                 |
| 3. <input type="checkbox"/> original general power of attorney  |           |                 |
| 4. <input type="checkbox"/> copy of general power of attorney; reference number, if any: .....  |           |                 |
| 5. <input type="checkbox"/> statement explaining lack of signature  |           |                 |
| 6. <input type="checkbox"/> priority document(s) identified in Box No. VI as item(s): .....   |           |                 |
| 7. <input type="checkbox"/> translation of international application into (language): .....   |           |                 |
| 8. <input type="checkbox"/> separate indications concerning deposited microorganism or other biological material  |           |                 |
| 9. <input type="checkbox"/> sequence listings in computer readable form (indicate type and number of carriers)  |           |                 |
| (i) <input type="checkbox"/> copy submitted for the purposes of international search under Rule 13ter only (and not as part of the international application):  |           |                 |
| (ii) <input type="checkbox"/> (only where check-box (b)(i) or (c)(i) is marked in left column) additional copies including, where applicable, the copy for the purposes of international search under Rule 13ter              |           |                 |
| (iii) <input type="checkbox"/> together with relevant statement as to the identity of the copy or copies with the sequence listings mentioned in left column  |           |                 |
| 10. <input type="checkbox"/> tables in computer readable form related to sequence listings (indicate type and number of carriers)   |           |                 |
| (i) <input type="checkbox"/> copy submitted for the purposes of international search under Section 802(b-quater) only (and not as part of the international application)  |           |                 |
| (ii) <input type="checkbox"/> (only where check-box (b)(ii) or (c)(ii) is marked in left column) additional copies including, where applicable, the copy for the purposes of international search under Section 802(b-quater) |           |                 |
| (iii) <input type="checkbox"/> together with relevant statement as to the identity of the copy or copies with the tables mentioned in left column   |           |                 |
| 11. <input type="checkbox"/> other (specify): .....   |           |                 |

Figure of the drawings which should accompany the abstract:  Language of filing of the international application: English

Box No. X SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE  
*Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).*



VAN REET Joseph

|   |   |
|---|---|
| For receiving Office use only   |   |
| 1. Date of actual receipt of the purported international application:   | 26 JUIN 2003 (26 -06- 2003)   |
| 3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application: |   |
| 4. Date of timely receipt of the required corrections under PCT Article 11(2):  |   |
| 5. International Searching Authority (if two or more are competent): ISA /  | 6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid |
| For International Bureau use only   |   |

Date of receipt of the record copy by the International Bureau:

**"Livestock products with an increased PPAR/RXR heterodimer activator level"**

The present invention relates to a non-therapeutic method for achieving an increased level of at least one PPAR/RXR heterodimer activator in a livestock product for human consumption, in particular in skeletal meat, milk and/or eggs, in which method livestock animals, used in agri- or aquaculture for producing the livestock product, are made to ingest at least one product comprising said PPAR/RXR heterodimer activator and/or a precursor thereof which is metabolised by the livestock animals into said PPAR/RXR heterodimer activator, over such a period of time and in such an amount that the PPAR/RXR heterodimer activator is accumulated in the livestock animal so that said increased PPAR/RXR heterodimer activator level is achieved in the livestock product.

An example of a PPAR/RXR heterodimer activator is conjugated linoleic acid (CLA). EP-A-1 106 077 discloses a method wherein a feed comprising extruded linseed is given to cows. This feed is intended to achieve milk having a particular content of saturated and unsaturated fatty acids and, in particular, an elevated CLA content. Other methods wherein the level of CLA in ruminant livestock products is enhanced through altering the dietary composition in the feeds such that more CLA is produced are disclosed in [Offer 1998] and in [Chilliard 2000]. CLA can also be supplemented directly to the feeds of other livestock such as pigs [Ostrowska 1999], poultry and fish in order to achieve enhanced levels of CLA in pork, chicken meat, eggs and fish meat.

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In the following table, a number of references disclosing CLA levels obtained by supplementing the feed of livestock animals with CLA are given. It displays per reference, the product targeted, the maximum level of CLA in the diet by weight and the maximum level of CLA found in that product as a percent of total fatty acids.

| Reference           | product      | max in diet | max of TFA         |
|---------------------|--------------|-------------|--------------------|
| Chamruspollert 1999 | egg yolk     | 5%          | 11,2%              |
| Shafer 2001         | egg yolk     | 2%          | 7.95%              |
| Raes 2002           | egg yolk     | 3%          | 5.3%               |
| Szymczyk 2001       | Chicken meat | 1.5%        | 10.27%             |
| Choi 1999           | Carp         | 1%          | 13%                |
| Twibell 2000        | striped bass | 0.6%        | 8.1%               |
| Twibell 2001        | yellow perch | 0.6%        | 2.92%              |
| Ramsey 2001         | lean pork    | 1.4%        | 3.2% (up to 55 kg) |
| Thiel-Cooper 2001   | lean pork    | 1%          | 0.7% (> 100 kg)    |
| Joo 2002            | lean pork    | 5%          | 1.6% (> 100 kg)    |

CLA is a fatty acid that has generated a lot of interest with respect to health since the discovery that grilled minced beef could inhibit carcinogenesis [Ha 1987]. During the last 15 years, numerous other physiological properties have been attributed to CLA beside it being anticarcinogenic [Belury 2002], including action as an antiadipogenic [Smedman 2001], antidiabetogenic [Houseknecht 1998, Ryder 2001] and antiatherosclerotic [Wilson 2000] agent. Furthermore CLA has effects on bone formation [Li 1999] and the immune system [Sugano 1998].

CLA stands for a group of positional and stereo-isomers of conjugated octadecadienoic acid, a fatty acid doubly unsaturated in positions separated by just one single bound and whereby one of the double bounds is in trans and the other in the cis steomeric configuration.

The natural source of CLA in foods is almost exclusively from ruminant livestock products like beef, lamb and dairy. The

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predominant isomer is c9t11-CLA. Several other isomers are also found such as t7,c9-CLA, c11t13-CLA, c8t10-CLA and t10c12-CLA [Fritzsche1999].

5       The synthetic production of CLA is usually based on an alkalinisation of a linoleic acid substrate. This process generates predominantly two isomers in roughly equal proportions: c9t11-CLA and t10c12-CLA [Reaney 1999]. The majority of the studies on CLA were performed with such a CLA isomer mixture.

10      In the general population, the intake of CLA has been estimated to vary widely between 15 - 659 mg/day [Park 1999]. As amounts as small as 0.5% of diet have been shown to alter expression of genes and impact conditions such as carcinogenesis, obesity, diabetes, and atherosclerosis in, mostly, animal studies, it is quite likely that these amounts taken over longer periods have similar benefits for the specific 15 human subgroups.

16      The mechanisms underlying the beneficial effects of CLA are slowly but surely being elucidated. One complicating factor is that the different CLA isomers seem to have some common and some different courses of action [Pariza 2001].

20      One line of action is based on the mediation of the peroxisome proliferator-activated receptor (PPAR). These are orphan nuclear receptors that require a dimerisation with a retinoid-X receptor (RXR) that when activated, straddle the peroxisome proliferator response elements (PPRE's) on the DNA to trigger the transcription of a particular 25 set of genes. PPARs come in three families alpha, beta (or delta) and gamma.

26      PPAR alpha is a PPAR family that is involved in the metabolism of fatty acids and lipoproteins. Synthetic activators of PPAR alpha include the lipid-lowering fibrates. These have been used for years 30 in clinical medicine to treat dyslipidemias. In addition, PPAR alpha

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activation improves insulin sensitivity and decreases inflammation in the vascular walls and thrombi. Each of these is an important factor in the onset, progression and complications of atherosclerosis. Furthermore, PPAR alpha ligands have been shown to prevent the induction and halt  
5 the progression of certain cancers in cell line and animal models. It has been shown that CLA is an agonist of PPAR alpha [Moya-Camarena 1999].

PPAR gamma is another PPAR family that is involved with adipogenesis and lipid metabolism. Thiazolidinediones (TZD) are potent  
10 insulin sensitizers used to treat type II diabetes. They were found to be synthetic ligands of PPAR gamma. In addition, PPAR gamma stimulation inhibits the production of a number of cytokines that are involved in promoting inflammation. Furthermore, the activation of PPAR gamma has been shown to prevent the induction of a number of cancers by  
15 promoting cell differentiation and stimulating apoptosis. It has been shown conclusively that CLA is an agonist of PPAR gamma [Houseknecht 1998, Yu 2002].

A second mode of action is through the inhibition of particular enzymes that elongate [Chuang 2001] and desaturate [Park  
20 2000] fatty acids. Although the impact of a mix of isomers of CLA, or of the individual isomers are not fully elucidated yet, it appears that CLA, through this mechanism, influences the level and character of cytokines derived from the LOX and COX fatty acid oxidation pathways [Urquhart 2002] and, consequently, impacts inflammation and blood clotting  
25 behavior.

Given the important potential health benefits of CLA, the required daily allowance has been calculated to be between 1.5 g and 3 g per day [Decker 1995]. As the present level of CLA in the diet is about three to ten times less than required, it became necessary to devise  
30 ways to supplement CLA in the human diet.

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Although CLA is a compound with a unique position in the human food chain and with interesting properties and potential for health promotion, it presents a number of important hurdles for its generalized supplementation in the human diet:

- 5    - CLA is represented by a variety of isomers exposing different and sometimes even opposite activities.
- The mechanisms of action of CLA are varied and influencing several different pathways simultaneously making it hard to elucidate the relative importance of each.
- 10   - As CLA joins the same pathways as linoleic acid and linoleic acid is a key-precursor for a couple of families of cytokines involved in the delicate balance in inflammation and clotting, the effect of CLA derived cytokines on this balance is worrisome.
- CLA supplementation decreases to a certain degree the effect of endogenous desaturases [Lee 1998]. This causes a serious shift in the fatty acid profile of foods from animal origin towards more of the less desirable saturated fatty acids.
- 15   - The large majority of studies have been using a mix of CLA isomers, complicating the interpretation of the mechanisms of action even more and casting serious doubt on any extrapolation.
- 20   - CLA is an unsaturated fatty acid and thus prone to oxidation [Hamalainen 2002], for example during cooking. Although CLA is relatively stable during storage and processing, the toxicological profile of its degradation products in foods remains elusive. In vivo, CLA has been shown to be reactive enough to, at least, induce lipid peroxidation products that are markers of arteriosclerosis [Basu 2000, Riserus 2002].
- 25   - The natural sources of CLA in the food chain are bacteria detoxifying a linoleic acid overload [Fukuda 2002]. The complete chemical synthesis of CLA is possible but not well established. The industrial production

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of CLA from plant based oils generates an unnatural mix of isomers [Saebo 2001]. Moreover, the isomer specific purification of CLA is far from trivial.

- 5 – In addition, it has been shown that CLA is produced endogenously from the trans monoene vaccenic acid [Adlof 2000] [Loor 2002]. This puts into question the necessity to supplement foods with CLA, in particular with isomers that are not generated by the mammalian organism itself.
- 10 – Furthermore, the association between CLA and a trans fatty acid like vaccenic acid complicates the interpretation of the conflict between the potential beneficial effects of CLA and the generally accepted noxious effects of trans fatty acids.
- 15 – Lastly, upto now there is little data about the effect of CLA in acute toxic and long-term lower level overload conditions.

An object of the present invention is to provide a new method for producing livestock products for human consumption which enables to achieve livestock products which also have interesting properties and potential for health promotion due to the presence of an increased level of a PPAR/RXR heterodimer activator but wherein a PPAR/RXR heterodimer activator or a precursor thereof different from CLA is used so that at least a number of the drawbacks of CLA indicated hereabove are obviated.

To this end, the method according to the present invention is characterised in that said PPAR/RXR heterodimer activator is phytanic acid, a metabolite of phytanic acid, a derivative of phytanic acid or of said metabolite, or a combination thereof and, in order to accumulate the PPAR/RXR heterodimer activator in the livestock animal, a predetermined amount of said product is given to the livestock animals over at least one period of at least three days, during which the livestock animals ingest a total amount of F kg feed dry weight, which

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predetermined amount of said product contains at least  $5 \times F$  meq, preferably at least  $10 \times F$  meq, and more preferably at least  $15 \times F$  meq of said PPAR/RXR heterodimer activator and/or precursor thereof.

Phytanic acid (PhA) is the common name for tetramethylhexadecanoic acid, a saturated fatty acid with four methyl branches. The PhA catabolism has been studied extensively for the last forty years, primarily, to explain the pathophysiology of Refsum's disease, a rare genetic disorder affecting the peroxisome metabolism [Verhoeven 2001]. In the late seventies, it was found that adhering to a low PhA diet could prevent the noxious accumulation of PhA and, soon, the PhA levels of foodstuffs were measured and specific dietary tables were established [Masters-Thomas 1980].

In the human diet, the most important sources of PhA are rumen products, such as from beef and dairy products, and fish products such as from herring, sardines and mackerel and the like. The PhA in these animals is the result of the uptake of phytol released during the breakdown of chlorophyll. Phytol is converted to PhA in the liver. PhA itself is broken down in pristanic acid (PrA) through an alpha-oxidation and subsequently in trimethyltetradecanoic acid (TMTD) through a beta-oxidation. Both these oxidations and the following two beta-oxidations occur in the peroxisome. The next ones occur in the mitochondrion.

In the rumen of ruminants, the chlorophyll contained in the forage grasses is broken down during the fermentation in the gut. The fish, on the other hand, obtain phytol by ingesting zooplankton that has been feeding on the phytoplankton. It is not generally known which microorganisms are responsible for hydrolyzing chlorophyll, neither in the rumen nor in the plankton.

After [Van den Branden 1986] noted that dietary phytol induced the proliferation of hepatic peroxisomes in adult mice, cell research showed that PhA is a ligand of RXR [Kitareewan 1996] and

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subsequently it was identified as a potent activator of PPAR alpha in physiologic concentrations [Ellinghaus 1999]. These characteristics point towards a number of promising human health claims such as against atherosclerosis [Pineda Torra 1999], non-insulin dependent diabetes 5 [Lenhard 2001] and cancer [Roberts-Thomson 2000]. As CLA had also been found to be an agonist of PPAR alpha [Moya-Camarena 1999] and PPAR gamma [Houseknecht 1998], some potential health benefits of CLA were hypothesized to pertain also to PhA.

In 2001, McCarty hypothesised that supplementing the 10 human diet with hydrolysed chlorophyll at a dosage of 0.5% of the diet weight in free phytol could be an effective prevention and treatment of non-insulin dependent diabetes [McCarty 2001]. He based his argument on the finding that cell research showed that some early phytol metabolites are a ligand of RXR [Kitareewan 1996] and that the 15 PPARgamma/RXR heterodimer was suggested as a target for treating diabetes [Mukherjee 1997]. As CLA was found to be an agonist of PPAR gamma [Houseknecht 1998], some health benefit claims of CLA could possibly extend also to phytol and its metabolites.

Although the potential beneficial effects of PhA are known 20 and although direct supplementation of the human diet with PhA or its precursor phytol has already been disclosed in [McCarty 2001], EP-A-1 177 789 and in WO-A-9709039, nobody has suggested up to the present invention any feeding strategy to enhance the level of phytol or its metabolites or derivatives thereof in food products of animal origin for 25 human consumption.

Compared to the above described disadvantages of the prior art methods wherein the human food is supplemented with CLA, the method according to the invention offers however the following advantages as a result of the use of PhA (or metabolites or derivatives 30 thereof) as PPAR/RXR heterodimer activator:

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- As PhA is completely saturated it does not present itself in different isomeric configurations, exposing possibly different activities like CLA isomers do.
- Although it cannot be excluded that PhA has other more subtle mechanisms of action, its main effect is evidently through its agonistic effect on the PPAR/RXR system.
- Although it cannot be excluded that PhA metabolises in other minor pathways, its main catabolic pathway has been completely elucidated in minute detail, together with a list of known genetic mutations that perturb this pathway.
- Although only relatively few PhA supplementation studies have been performed, their interpretation is not complicated by a mixture of compounds with possible opposing activities like with CLA.
- As PHA is fully saturated there is no inherent problem of oxidation. This means that the compound is not only stable during storage, processing and heating, but that also we do not expect in vivo reactions such as lipid peroxidation that cast doubt over CLA as a potential healthy supplement.
- The natural source of PhA is the chlorophyll used in plants and algae. The complete synthetic chemical synthesis is well established [Eldjarn 1966] and is the preferred industrial method to produce precursors of vitamins such as vitamin K and vitamin E. The industrial production of PhA from plant-based material is also relatively trivial.
- As there is no endogenous production of PhA from any lower level precursor in the animal kingdom, all PhA in the organism is of dietary origin. This eliminates the uncertainty about influences of other precursors like trans vaccenic acid does with in CLA studies.
- As Refsum patients have been studied thoroughly, we have extensive information about the metabolic effects of long term toxic doses.

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Direct supplementation of the human or animal diet with phytol or phytanic acid has already been disclosed in the prior art but only for therapeutic purposes. EP-A-1 177 789 discloses the therapeutic use of PhA or phytol for the treatment or prevention of diabetes whilst in 5 WO-A-9709039, PhA is described to be a vitamin, more particularly vitamin F, which can be used for treating vitamin F deficiency. Vitamins are however used in very small, trace concentrations and are never meant to accumulate in tissues. Moreover, also in EP-A-1 177 789, the phytanic acid or phytol is administered in relatively small daily doses, 10 more particularly in daily doses of between 0.1 and 50 mg/kg body weight, and usually of between 0.5 and 40 mg/kg body weight. Although EP-A-1 177 789 mentions the use of phytol or phytanic acid for preventing or treating diabetes in humans or animals, it does not teach any specific animals and a skilled person would not use it for livestock 15 animals since these animals do not suffer from diabetes that warrants treatment. Moreover, EP-A-1 177 789 does not teach to supplement feed with phytol or phytanic acid to achieve an accumulation of phytanic acid in the livestock products, no tissue concentrations being indicated at all.

In other prior art documents, the accumulation of PhA in 20 certain tissues has been mentioned.

Lough [Lough 1977] has noted the possible effect of natural feeds (containing chlorophyll) on the level of PhA in the liver, kidney, heart, brain, omental fat, plasma and milk in a dozen of cows and steers. However, this method is not in accordance with the present invention 25 since the grass silage fed in these experiments contained only a relatively small amount of chlorophyll. Moreover, chlorophyll can only be broken down in ruminants so that feeding chlorophyll to non-ruminants will have no significant effect on the PhA content.

In contrast to chlorophyll, phytol can be metabolised in non- 30 ruminants. In the prior art, only laboratory animals have, however, been

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supplemented with phytol, primarily to elucidate the pathophysiology of Refsum's disease. In general, it was moreover noted that substantial morbidity as evidenced by growth retardation, weight loss and lethargy, already emerged from levels of supplementation of 1% of diet weight on 5 and serious mortality rates were induced at levels of 5% [Steinberg 1966].

From the prior art it thus appears that phytol supplementation has such toxic effects on growth and health in laboratory animals that [Steinberg 1966] concluded, albeit within the 10 context of the development of an animal model for Refsum's disease, that "the dosages of dietary phytol or phytanic acid needed to produce tissue accumulation of phytanic acid in normal animals are large and incompatible with growth and survival in the species tested."

According to the invention it was found that, under standard 15 zoo technical conditions, it appeared to be possible to achieve increased levels of PhA (or metabolites or derivatives thereof) in livestock products by supplementing the feed of livestock animals with phytol or other compounds forming or producing the above described PPAR/RXR heterodimer activator, more particularly, increased levels that have a 20 beneficial effect on the health of the humans consuming the livestock products. This is quite surprising not only in view of the toxic effects of phytol but also in view of the fact that the branched nature of PhA seriously impedes the activity of several fatty acid enzymes that do not seem impacted as much by CLA. As indirect evidence, it was already 25 noted that the presence of PhA in substantial proportion in the triglycerides and phospholipids was associated with the presence of phytanic acid (and not PhA) in the cholesterol esters of plasma [Steinberg 1966] but not with its deposition in quantity in a series of tissues. For example, PhA apparently inhibits the adipose tissue 30 lipoprotein lipase, blocking its significant deposition in fat tissue. Also the

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mammary gland lipoprotein lipase discriminates against PhA, severely limiting the deposition of PhA in the milk, despite high plasma levels. Illustrative is also that the placental barrier is virtually impermeable to PhA [Lough 1977].

Consequently, one cannot extrapolate the deposition rate of PhA in the egg, for example, nor in the skeletal muscle of the growing organism. Granted, the deposition of PhA in the heart of grass fed steers was significant [Lough 1977]. Indeed, as the heart muscle is constantly active, it has an excessive and continuous energy requirement in contrast to other muscle types. As most of the energy is provided by fatty acids, the heart muscle has a very high turn over rate of its fatty acids. Consequently, dietary changes are more readily reflected in the fatty acid profile of the heart muscle, even if a particular compound, like PhA, is far from being the preferred substrate. However, skeletal muscles have much lower energy requirements and their main energy source is glycogen, not fatty acids. Therefore, the turn over rate of fatty acids in skeletal muscle is manyfold lower than that for the heart muscle and their metabolic enzymes are under a substantially different tissue specific control and configuration.

In the method according to the invention; the human diet is supplemented with a PPAR/RXR heterodimer activator in order to achieve beneficial health effects. The PPAR/RXR dimer activator is an agonist of any of the PPARs alpha and gamma and/or of the RXR enabling to activate the PPAR/RXR dimer so that it may straddle the peroxisome proliferator response elements (PPRE) on the DNA to trigger the transcription of a particular set of genes. The PPAR/RXR heterodimer activator employed in the present invention is phytanic acid, a metabolite of phytanic acid, a derivative of phytanic acid or of said metabolite, or a combination thereof. The PPAR/RXR heterodimer activator is advantageously phytanic acid, pristanic acid, TMTD (4,8,12-

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trimethyltridecanoic acid), a derivative of these acids or a combination thereof, the PPAR/RXR heterodimer activator being preferably phytanic acid and/or pristanic acid.

In the method according to the invention, the level of one or more of these PPAR/RXR heterodimer activators is increased in livestock products, in particular in skeletal meat, milk and/or eggs, produced by livestock animals in agri- or aquaculture. This is achieved by making the livestock animals ingest at least one product that comprises the PPAR/RXR heterodimer activator and/or a precursor thereof, which is metabolised by the livestock animals into the PPAR/RXR heterodimer activator. The product can be in the form of a feed or a feed supplement fed to the animals (either via the feed or via the drinking fluids). An important advantage of the method according to the invention is that, by feeding the product to livestock animals instead of directly to humans, the human food itself is rendered more healthy but with at least one order of magnitude lower risk of overload, overdoses or adverse effects for the consumers.

When the livestock animals are ruminants, chlorophyll can be given as precursor of the PPAR/RXR heterodimer activator. This chlorophyll is preferably contained in a chlorophyll rich product containing at least 0.25% by dry weight, preferably of at least 0.50% by dry weight and more preferably of at least 0.75% by dry weight chlorophyll. Examples of such chlorophyll rich products are chlorophyll paste, Chlorella powder, dried blue green algae, Spirulina/Chlorella powder or tablets and Spirulina. Chlorophyll given in a less concentrated form contributes however also to the accumulation of the PPAR/RXR heterodimer activator. Consequently, grass, grass silage, alfalfa (which contains more chlorophyll than grass) and other natural feeds can be given, in combination with a product which has a higher content of the

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PPAR/RXR heterodimer activator and/or the precursor thereof in order to achieve the minimum amounts required by the invention.

Non-ruminants can be given metabolites of chlorophyll, i.e. first of all, phytol, which further metabolises into phytanic acid, pristanic acid and TMTD. In view of the cost for producing it on an industrial scale, phytol is the preferred product to be given to the livestock animals in the present economic conditions. The other compounds are more expensive to produce per PPAR/RXR heterodimer activator equivalent, but can also be used in the method according to the invention. Possibly, use can be made of living organisms containing a relatively high level of these compounds, for feeding the livestock. On the other hand, chlorophyll can also be given to non-ruminants together with chemical or biological agents that are active to dissociate the phytol chain from its chlorophyll parent molecule.

Instead of administering the above compounds respectively in the alcohol and in the acid form, they can also be administered in the form of a salt, an ester or an amide since these compounds will be converted back to the alcohol or the acid form in the gastro-intestinal system.

More generally, different derivatives of the above compounds and metabolites of phytol can be used provided they act as PPAR/RXR heterodimer activator or provided they are a precursor of such an activator in the livestock animals. Such compounds can be selected from the group of compounds corresponding to the following formulas:

CH<sub>3</sub>-CR<sub>1</sub>H-CH<sub>2</sub>-CH<sub>2</sub>-CR<sub>2</sub>H-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CR<sub>3</sub>H-CH<sub>2</sub>-CH<sub>2</sub>-(CH<sub>2</sub>)<sub>m</sub>-R<sub>4</sub>  
and CH<sub>3</sub>-CR<sub>1</sub>H-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CR<sub>2</sub>H-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CR<sub>3</sub>H-R<sub>5</sub>,  
wherein:

each of R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and R<sub>6</sub> is either CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub> or C<sub>3</sub>H<sub>7</sub>;

m = 0 - 2;

R<sub>4</sub> = CH<sub>2</sub>-CR<sub>6</sub>=CH-CH<sub>2</sub>OH (phytol);

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- CH<sub>2</sub>-CR<sub>6</sub>=CH-CHO (phytenal);  
CH<sub>2</sub>-CR<sub>6</sub>=CH-COOH (phytenic acid);  
CH<sub>2</sub>-CR<sub>6</sub>H-CH<sub>2</sub>-COOH (phytanic acid);  
CH<sub>2</sub>-CR<sub>6</sub>H-CHOH-COOH (2-hydroxyphytanic acid);  
5 CH<sub>2</sub>-CR<sub>6</sub>H-CH<sub>2</sub>-CH<sub>2</sub>OH;  
CH<sub>2</sub>-CO-CH<sub>2</sub>-COOH;  
CH<sub>2</sub>-CR<sub>6</sub>H-COOH (pristanic acid);  
CHOH<sub>2</sub>-CR<sub>6</sub>H-COOH (3-hydroxypristanic acid);  
CH<sub>2</sub>-CR<sub>6</sub>H-CH<sub>2</sub>-CH<sub>2</sub>OH;  
10 CH<sub>2</sub>-CR<sub>6</sub>H-CHO (pristanal);  
CH=CR<sub>6</sub>-COOH (2, 3 pristenic acid);  
CO-CR<sub>6</sub>H-COOH (3 keto pristanic acid);  
CH<sub>2</sub>-CHOH-CH<sub>2</sub>OH;  
CH<sub>2</sub>-CO-COOH;  
15 CH<sub>2</sub>-COOH;  
CH<sub>2</sub>-CHO;  
CH<sub>2</sub>-CH<sub>2</sub>OH;  
CHOH-CH<sub>2</sub>OH;  
CH<sub>2</sub>-O-CHO;  
20 COOH (4,8,12-TMTD); or  
CHO and  
R<sub>5</sub> = CH<sub>2</sub>-COOH or  
COOH,

or which are a salt, an ester or an amide thereof, in particular chlorophyll,  
25 prophyrin, and phospholipid and di- or triacylglycerol esters. The names  
between brackets are the names of the respective compounds when m =  
0 and R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and optionally R<sub>6</sub> is CH<sub>3</sub>.

In the method according to the invention the product  
comprising the PPAR/RXR heterodimer activator or the precursor thereof  
30 is given in a predetermined minimum amount and for a period of time

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such that the PPAR/RXR heterodimer activator accumulates in the livestock animal and an increased level is obtained in the livestock product. The minimum amount of activator to be given over a period of at least three days is expressed as a ratio of the amount feed dry matter ingested by the livestock animals during that period. In order to exclude any effect of the molecular weight of the activator or precursor and in order to exclude the effect of any difference in the number of functional activator groups in the precursor, the amount of activator is further expressed in milli-equivalents, more particularly in PPAR/RXR heterodimer activator milli-equivalents. One millimole of phytol, i.e. 294 mg of phytol, thus corresponds to one meq phytol. For example, when a precursor is used such as a di- or a triglyceride containing two or three phytanate groups, one mole corresponds to two or respectively three equivalents of the di- or the triglyceride.

When the livestock animals eat a total amount of  $F$  kg feed dry weight over said period of time, they should be made to ingest an amount of the product which contains at least  $5 \times F$  meq, preferably at least  $10 \times F$  meq, and more preferably at least  $15 \times F$  meq of said PPAR/RXR heterodimer activator and/or precursor thereof. When different activators and/or precursors are used, the sum of the respective amounts of these compounds should be greater than the minimum amount, provided the different compounds are available for the livestock animal, i.e. provided the compounds can be taken up and, if necessary, converted into the PPAR/RXR dimer activator. When phytol is used, the above amounts correspond to about 0.15, 0.3 and 0.45% of dry diet weight, respectively.

During said period of time, the product can be given one or several times. Preferably, the product is given at least once a day and is more preferably given with the feed of the livestock animals. The product can be given separately from the feed but preferably it is mixed therewith.

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The present invention also provides a feed for livestock animals which is composed to contain at least 5 meq/kg feed dry weight, preferably at least 10 meq/kg feed dry weight, and more preferably at least 15 meq/kg feed dry weight of the PPAR/RXR heterodimer activator and/or precursor

5 thereof, preferably phytol. This feed can either be manufactured in advance or the farmer can also prepare it by mixing a product containing the PPAR/RXR heterodimer activator and/or precursor thereof with other feed constituents. Optionally, the product can also be administered via the drinking fluids.

10 The product is preferably given in said amounts over more than one period of at least three days or over one or more longer periods, more particularly over at least one period of at least one week, more preferably over at least one period of at least two weeks so that it further accumulates in the livestock animal. When the livestock animals are  
15 slaughtered to produce the livestock product, in particular skeletal meat, the livestock animals are made to ingest the product preferably for at least three days during the last week before slaughtering. Of course, the product can already been given before the last week and also during the entire last week. During the last days, it can moreover be given in an  
20 increased amount in order to achieve a maximum level in the livestock product upon slaughtering.

Compared to the therapeutic amounts of phytol and phytanic acid, the amounts given in accordance with the present invention are relatively high, and are, in particular, considerably higher  
25 than the amounts which can be achieved by feeding grass or even alfalfa to ruminants. For a pig of 80 kg having a daily dry feed intake of 2 kg, the amounts of 5 x F meq, 10 x F meq and 15 x F meq correspond to 37 mg, 74 mg and 111 mg/kg body weight, respectively. For a chicken of 2 kg having a daily dry feed intake of 0.1 kg, these amounts correspond even  
30 to 74 mg, 148 mg and 222 mg/kg body weight, respectively. In order to

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achieve an even higher accumulation of the PPAR/RXR heterodimer activator, the livestock animals can be made to ingest, over said period of time, at least  $25 \times F$  meq, preferably at least  $35 \times F$  meq, more preferably at least  $50 \times F$  meq and most preferably at least  $65 \times F$  meq of the  
5 PPAR/RXR heterodimer activater and/or precursor thereof. When phytol is used, these amounts correspond to about 0.75, 1.0, 1.5 and 2.0% of dry diet weight, respectively. Preferably, the livestock animals are made to ingest, over said period of time, less than  $175 \times F$  meq, and more  
10 preferably less than  $125 \times F$  meq of the PPAR/RXR heterodimer activater and/or precursor thereof.

By means of the method according to the invention, livestock products can be produced having certain minimum levels of the PPAR/RXR heterodimer activator, in particular of phytanic acid, pristanic acid and/or TMTD, by giving the products containing this or these  
15 activators and/or precursors thereof in a sufficiently large amount and for a sufficient long period of time.

In the present specification the level of the PPAR/RXR heterodimer activator is expressed as a percentage of total FAME fatty acids. These total FAME fatty acids comprise those fatty acids with a  
20 linear chain of at least 12 carbons and are measured by the so-called FAME technique, which is well known for the skilled person and wherein, first, fatty acid methyl esters are prepared which are, subsequently, analysed via gas chromatography. The FAME procedure used for determining the results obtained by the present invention was as follows.  
25 Lipids were extracted from the samples using a dissolving solution that is specific to each sample type. Nonadecanoic acid (19:0) was added as an internal standard. The two-step methylation procedure consisted of using a basic reagent NaOH/methanol followed by an acid reagent HCl/methanol. The fatty acid methyl esters (FAME) were analyzed by GC  
30 (HP 6890, Hewlett-Packard, Brussels, Belgium) using a CP-Sil88 column

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for FAME (100 m x 250 µm x 0.25 µm) (Chrompack, Middelburg, The Netherlands). The GC conditions were as adapted to each sample type. Peaks were identified by comparison of retention times with those of the corresponding standards (Sigma, Botnew, Belgium; Nu-Chek-Prep, 5 Elysian, MN). Identification of the peaks included fatty acids between 12:0 and 22:6 and 5 different CLA isomers and phytanic acid and pristanic acid.

The product can be given to non-ruminant mammals and to poultry (broilers) so that a level of said PPAR/RXR heterodimer activator of at least 0.2%, preferably of at least 0.5% and more preferably of at 10 least 1.0% of total FAME fatty acids is achieved in said livestock product, in particular, in skeletal meat of the livestock animals. The non-ruminant mammals are preferably non-rodents since it has been found that non-rodents, generally, do not show the peroxisome proliferation upon 15 activation of the PPAR/RXR heterodimer that is typical in laboratory mice.

When the product is given to poultry (layers) producing eggs as the livestock product, the product is preferably given so that a level of said PPAR/RXR heterodimer activator of at least 1%, preferably of at least 3% and more preferably of at least 5% of total FAME fatty acid 20 is achieved in egg yolk of said eggs.

When the product is given to ruminants producing skeletal meat as the livestock product, the product is preferably given so that a level of said PPAR/RXR heterodimer activator of at least 0.7%, preferably of at least 0.9% and more preferably of at least 1.0% of total 25 FAME fatty acid is achieved in skeletal meat of the livestock animals.

When the product is given to ruminants producing milk as the livestock product, the product is preferably given so that a level of said PPAR/RXR heterodimer activator of at least 0.75%, preferably of at

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least 1.0% and more preferably of at least 1.5% of total FAME fatty acid is achieved in milk of the livestock animals.

When the product is given to aquatic animals such as the aquatic animals defined in the main group 4 "Fish and fish products" of 5 the Europcode 2 version of 4/8/99, which are incorporated herein by way of reference, used to produce the livestock product in aquaculture, the product is preferably given so that a level of said PPAR/RXR heterodimer activator of at least 0.7%, preferably of at least 0.9% and more preferably of at least 1.0% of total FAME fatty acid is achieved in the livestock 10 product.

The method according to the invention cannot only be applied to accumulate the PPAR/RXR heterodimer activator in livestock products but it also enables to improve the carcass quality of livestock animals. In particular for pigs, it has been observed that, from a group of 15 pigs that were given phytol, a number of pigs did no longer gain weight but exhibited a carcass configured towards more lean mass.

Experiments have also shown that, for some kinds of livestock animals, the supplementation of the feed with the PPAR/RXR heterodimer activator or the precursor thereof has, within a population of 20 the same livestock animals, a different effect on a certain parameter so that the population can be split up into two groups. For chicken (broilers) it has for example be observed that the feeding of phytol causes in one group of chicken a greater accumulation of phytanic acid than in the other group. A selection can thus be made for chicken showing the 25 largest accumulation of PhA. For pigs, it has on the other hand been observed that, within one population, there were two groups, namely one group which fails to gain weight when being made to ingest phytol whilst another group gained weight to a comparable extend as a control group. When, as explained hereabove, an improved carcass quality is the 30 production goal, one should continue the phytol administering to the

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group of pigs that do not gain weight whilst when only an accumulation of the PPAR/RXR heterodimer activator is the production goal, one should continue with the group of pigs which gained weight.

Example 1: broilers

5 ROSS 308 broiler chicks were raised, lege artis, on an ad libitum diet, containing phytol at 2% by weight of feed that, characteristically, contains about 10% of humidity. The chicks consumed an average of about 0.1 kg dry weight of the feed per day. The phytol in the diet replaced 2% of the soybean oil included in feeds formulated  
 10 based on the INVE Nutritional Requirement standard formula for a grower feed (formula 120). Please refer to the following tables for the feed formula and for its chemical composition.

*Broiler feed composition*

|       |                           | Composition (%) |
|-------|---------------------------|-----------------|
| 300   | Corn                      | 26.00           |
| 800   | Wheat                     | 28.70           |
| 1402  | Fullfat soybeans, toasted | 17.00           |
| 1424  | Soybean meal 48+2         | 17.00           |
| 2815  | Patatoprotein             | 2.20            |
| 4200  | Soybean oil               | 2.00            |
| 4370  | INVE fat                  | 3.70            |
| 5100  | Monocalciumphosphate      | 0.97            |
| 5150  | Limestone                 | 0.87            |
| 5170  | Salt                      | 0.28            |
| 5173  | Sodiumbicarbonate         | 0.27            |
| 5300  | L-lysine                  | 0.17            |
| 5301  | DL-Methionin              | 0.24            |
| 5303  | L-threonine               | 0.05            |
| 6511  | Sacox 12%*                | 0.05            |
| 84928 | INVE Broiler 0.5 %        | 0.50            |
|       | Sum                       | 100.00          |

*Chemical composition of broiler feed*

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|                        | Composition<br>(g/kg) |
|------------------------|-----------------------|
| Dry matter             | 889                   |
| Crude ash              | 81                    |
| Crude protein          | 212                   |
| Fat                    | 106                   |
| Starch                 | 344                   |
| Crude fibres           | 31                    |
| Ca                     | 8.0                   |
| Total P                | 5.4                   |
| Av. P                  | 4.0                   |
| Ca / Av.P              | 2.0                   |
| <br>Dig lysine poultry | 11.0                  |
| Dig met/dig lys        | 0.47                  |
| Dig met+cyst/dig lys   | 0.73                  |
| Dig thr/dig lys        | 0.65                  |
| Dig try/dig lys        | 0.21                  |
| <br>MEn broiler (kCal) | 3021                  |
| MEn broiler (kJ)       | 12.6                  |
| MEn poultry (kCal)     | 3259                  |
| MEn poultry (kJ)       | 13.6                  |

The animals were slaughtered after 42 days and their tissues sampled for analysis.

During the feeding trial, there was no difference in mortality or morbidity when compared with a group that received the standard broiler feed without the phytol supplement. It was observed that the final body weight (2122 g vs. 1842 g), the feed conversion rate (1.818 vs. 5 2.120) and the ratio breast weight/total weight (15.9% vs. 14.4%) were roughly one tenth less advantageous under the phytol supplementation diet, but still well within acceptable zoo technical ranges.

10 The fatty acid analysis of breast meat showed that PhA reached an average level of 2.6% of total fatty acids. Noteworthy was also a serious drop in PUFA (polyunsaturated fatty acid) content that is

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explained by the lack of 2% of soybean oil in the phytol supplemented diet.

Closer inspection of the results revealed that the broilers in the treatment group could be classified neatly into two subgroups according to the content of PhA in the breast meat, with values of one subgroup clustered around 1.9% and the values of the other subgroup clustered around 3.6%, almost double. This illustrates clearly the emergence of a heretofore silent phenotype under conditions that put the metabolic pathway of PhA under heavier loads. If the initial weight gain is correlated with this final PhA deposition rate, a selection is possible by phenotype after a short feeding trial to continue the finishing with those individual animals with the most effective phenotype.

#### Example 2: layers

48 week old ISABROWN layers were kept, lege artis, and fed ad libitum a diet containing phytol at 2% by feed weight. The layers consumed on average about 0.1 kg dry weight of the feed a day. The phytol replaced 2% of soybean oil included an INVE layer formulation with the following feed composition.

#### *Layer feed composition*

|       |                           | Composition (%) |
|-------|---------------------------|-----------------|
| 300   | Corn                      | 45.50           |
| 800   | Wheat                     | 20.00           |
| 1402  | Fullfat soybeans, toasted | 22.00           |
| 4200  | Soybean oil               | 2.00            |
| 5100  | Monocalciumphosphate      | 0.77            |
| 5150  | Limestone                 | 2.20            |
| 5152  | Limestone SEM white       | 6.50            |
| 5170  | Salt                      | 0.23            |
| 5173  | Sodiumbicarbonate         | 0.18            |
| 5301  | DL-Methionin              | 0.12            |
| 84928 | INVE Broiler 0.5 %        | 0.50            |

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|  |     |        |
|--|-----|--------|
|  | Sum | 100.00 |
|--|-----|--------|

There was no difference in mortality nor morbidity in comparison with a group fed a standard layer diet without phytol supplementation. Although the daily egg mass was lower with the 5 supplemented diet, the feed conversion rate remained zo technically within acceptable ranges. This is shown in this table below:

|               | Laying rate<br>(%) | Egg weight<br>(g/a/d) | Daily egg mass<br>(g/a/d) | ADFI<br>(g/a/d) | FCR |
|---------------|--------------------|-----------------------|---------------------------|-----------------|-----|
| control       | 90.3               | 65.6                  | 59.2                      | 112.3           | 1.9 |
| 2% phytol fed | 83.0               | 62.8                  | 52.1                      | 103.8           | 2.0 |

The quality of the eggs with respect to standard parameters for shell quality and color of the yolk did not change significantly except 10 for a less reddish coloring of the yolk in the supplemented group. The fatty acid analysis of the egg yolk revealed that supplementing the diet with 2% by weight phytol resulted in a deposit of 11.5 % of total FAME fatty acids of the branched chain fatty acids PhA, mainly, and a trace of PrA. Surprisingly, it appeared that the PhA displaced almost exclusively 15 the mono unsaturated fatty acids.

#### Example 3: pork

Hybrid boars weighing in at about 80 kg were kept lege artis and fed a standard finishing granulated feed sprayed on with phytol at a level of 2% of feed weight. The feed was formulated and produced by 20 Schatteman in Wetteren, Belgium and contained on average about 7% of humidity. On spraying, the feed readily absorbed this oily substance. The boars were fed the phytol supplemented granulated feed ad libitum and consumed on average about 1.8 kg of this feed per day. After one month, the boars were slaughtered. Tissue samples were taken and the carcass 25 quality assessed. The carcasses were further butchered in the usual

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fashion to chops, loins, sausages and the like and the meat quality of the prime cuts was assessed.

During the finishing period no difference in feeding behavior or level of activity was observed between the boars fed the usual diet and those fed the phytol enriched feed. Also, no animals got sick or died during the entire period. At slaughter, the boars in the intervention group could be divided into two groups according to their slaughter weight: a group which thrived and gained weight comparable to boars which had received the standard diet (weight gain 13.1 vs 11.2 kg) and another group which thrived but failed to gain weight. We presume that, as is usual in pig rearing, genetic variability accounts for these differences. Obviously, in practice, one could introduce a feed trial for a week and continue on with the supplemented diet only with those animals that showed already a significant weight gain or select those prone to carcass fat to lean mass redistribution to increase the carcass quality.

|                    | initial weight | final weight | % meat | type-index | quality class | chinese color | moisture loss |
|--------------------|----------------|--------------|--------|------------|---------------|---------------|---------------|
| control group      | 80000          | 91500        | 60.88  | 1.79       | A1            | 2.50          | 0.045         |
|                    | 81000          | 95000        | 57.61  | 2.25       | A2            | 3.00          | 0.043         |
|                    | 88000          | 99500        | 51.32  | 2.54       | B2            | 2.50          | 0.085         |
|                    | 79000          | 94500        | 59.42  | 2.07       | A1            | 2.00          | 0.067         |
|                    | 80000          | 93000        | 57.99  | 2.42       | B2            | 2.50          | 0.067         |
| 2% phytol group    | 82000          | 91500        | 56.38  | 1.93       | A2            | 2.50          | 0.065         |
|                    | 80000          | 77500        | 58.89  | 2.3        | A1            | 3.50          | 0.031         |
|                    | 87500          | 83000        | 60.62  | 1.83       | A1            | 2.50          | 0.039         |
| average control    | 82000          | 95125        | 57.31  | 2.16       |               | 2.50          | 0.060         |
| average 2% phytol  | 82375          | 86250        | 58.47  | 2.12       |               | 2.75          | 0.050         |
| average gainers    | 81000          | 92250        | 57.19  | 2.18       |               | 2.50          | 0.066         |
| average no-gainers | 83750          | 80250        | 59.76  | 2.07       |               | 3.00          | 0.035         |

With respect to the quality of the carcasses and the meat, no significant differences were found with those fed the standard diet. The quality was assessed objectively using the following parameters: % meat on the carcass, type-index, meat class, meat moisture, meat color, meat temperature and meat pH change. It was remarkable that the group that failed to gain weight produced top quality, lean and good muscled carcasses (quality class A1).

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| color          | control group |         |         |            | 2% phytol group |       |       | average control | average 2% phytol |
|----------------|---------------|---------|---------|------------|-----------------|-------|-------|-----------------|-------------------|
|                | L (avg)       | a (avg) | b (avg) | 40 minutes |                 |       |       |                 |                   |
| pH L carré     | 5.94          | 6.14    | 6.02    | 6.00       | 5.83            | 5.88  | 5.95  | 6.01            | 6.03              |
| pH R carré     | 6.14          | 6.13    | 5.99    | 5.84       | 5.70            | 5.84  | 6.01  | 5.90            | 6.03              |
| pH L ham       | 6.17          | 5.87    | 6.19    | 5.98       | 5.95            | 6.40  | 5.93  | 6.09            | 6.05              |
| pH R carré     | 6.29          | 5.90    | 6.13    | 6.01       | 5.72            | 6.51  | 5.90  | 6.98            | 6.08              |
| T L carré (°C) | 37.80         | 38.90   | 40.70   | 37.90      | 39.60           | 40.20 | 38.70 | 39.00           | 38.83             |
| T T carré (°C) | 37.80         | 39.70   | 40.60   | 37.60      | 38.10           | 39.80 | 39.00 | 39.40           | 39.08             |
| 24 hours       |               |         |         |            |                 |       |       |                 |                   |
| pH L carré     | 5.30          | 5.27    | 5.16    | 5.21       | 5.18            | 5.19  | 5.33  | 5.18            | 5.24              |
| pH R carré     | 5.29          | 5.21    | 5.28    | 5.19       | 5.16            | 5.18  | 5.29  | 5.31            | 5.24              |
| pH L ham       | 5.29          | 5.31    | 5.33    | 5.25       | 5.35            | 5.29  | 5.32  | 5.29            | 5.30              |
| pH R carré     | 5.33          | 5.37    | 5.41    | 5.28       | 5.29            | 5.29  | 5.33  | 5.28            | 5.30              |

With respect to the further processing of the pork, there were no noticeable differences in handling and transforming the meat.

With respect to the content of PhA and PrA in the pork meat, levels averaging 2.3% of total FAME fatty acids were found. It was also remarkable that the inclusion of these branched chain fatty acids did not produce a significant shift in the remainder of the fatty acid profile like towards less unsaturated fatty acids as is commonly found in CLA supplementation experiments.

10

#### Example 4: shrimp

Tiger shrimp (*Penaeus Monodon*), weighing in at 0.7 g a piece, were kept lege artis and fed a diet containing phytol at 2% of pellet diet weight and this during 4 weeks. The feeds were extruded using a standard shrimp grow out recipe as developed by INVE Technologies nv, Dendermonde, Belgium, where the phytol replaced 2% of soybean oil. The shrimp were allocated 20 a piece in triplicate tanks of 500 liters. After a week of acclimatization the shrimp were fed at a daily rate of about 15% of biomass weight.

15

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**Formula shrimp finishing**

|                        |        |        |
|------------------------|--------|--------|
| Wheat Flour            | 43.319 | 43.319 |
| Fish Meal Standard 999 | 35.000 | 35.000 |
| Defatted Soya Flour 50 | 9.610  | 9.610  |
| Shrimphead Meal        | 4.000  | 4.000  |
| Wheat Gluten           | 2.000  | 2.000  |
| Soya Oil               | 2.000  | 0.000  |
| Phytol                 | 0.000  | 2.000  |
| Squid meal             | 1.000  | 1.000  |
| Brewers Yeast          | 0.750  | 0.750  |
| Lecithin               | 0.679  | 0.679  |
| Fish Oil               | 0.642  | 0.642  |
| INVE Premix            | 1.000  | 1.000  |
|                        | 100.0  | 100.0  |

**Proximate Analysis (% in diet)**

|                            |       |       |
|----------------------------|-------|-------|
| Moisture                   | 10.20 | 7.37  |
| Crude Protein              | 38.00 | 39.53 |
| Crude Fibre                | 1.20  | 1.23  |
| Crude Ash                  | 8.02  | 8.35  |
| Crude Fat after Hydrolysis | 8.80  | 8.37  |

At the end of the feeding trials, there was no difference in survival rate compared with a similar triplicate group fed the standard diet without phytol supplementation. The delay on growth in the supplemented diet group was marked but still satisfactory from a zootechnical point of view (2.05 g vs. 3.3 g). During the first two weeks of feeding, the consumption of feeds in both groups was similar, although the growth rate differed already at about the same proportion. During the last two weeks however, the supplemented diet group consumed considerably less feed (53.7 vs 66.5 g), thus partially correcting an initially less attractive feed conversion ratio. Moreover, the shrimps used in this example were quite young, for more adult shrimp, the delay on growth is expected to be even smaller.

15 Fatty acid analysis revealed that during that feeding period the shrimp tissue had accumulated an average of 5.3% of TFA (total fatty

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acids) of PhA. Also, the total fat content dropped with about a fifth, a potential marketing advantage.

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CLAIMS

1. A non-therapeutic method for achieving an increased level of at least one PPAR/RXR heterodimer activator in a livestock product for human consumption, in particular in skeletal meat, milk and/or eggs, in which method livestock animals, used in agri- or aquaculture for producing the livestock product, are made to ingest at least one product comprising said PPAR/RXR heterodimer activator and/or a precursor thereof which is metabolised by the livestock animals into said PPAR/RXR heterodimer activator, over such a period of time and in such an amount that the PPAR/RXR heterodimer activator is accumulated in the livestock animal so that said increased PPAR/RXR heterodimer activator level is achieved in the livestock product, characterised in that said PPAR/RXR heterodimer activator is phytanic acid, a metabolite of phytanic acid, a derivative of phytanic acid or of said metabolite, or a combination thereof and, in order to accumulate the PPAR/RXR heterodimer activator in the livestock animal, a predetermined amount of said product is given to the livestock animals over at least one period of at least three days, during which the livestock animals ingest a total amount of  $F$  kg feed dry weight, which predetermined amount of said product contains at least  $5 \times F$  meq, preferably at least  $10 \times F$  meq, and more preferably at least  $15 \times F$  meq of said PPAR/RXR heterodimer activator and/or precursor thereof.

2. A method according to claim 1, characterised in that said product comprises as said PPAR/RXR heterodimer activator or as said precursor thereof at least one compound selected from the group of compounds which correspond to the following formulas:

$\text{CH}_3\text{-CR}_1\text{H-CH}_2\text{-CH}_2\text{-CH}_2\text{-CR}_2\text{H-CH}_2\text{-CH}_2\text{-CH}_2\text{-CR}_3\text{H-CH}_2\text{-CH}_2\text{-(CH}_2\text{)}_m\text{-R}_4$   
and  $\text{CH}_3\text{-CR}_1\text{H-CH}_2\text{-CH}_2\text{-CH}_2\text{-CR}_2\text{H-CH}_2\text{-CH}_2\text{-CH}_2\text{-CR}_3\text{H-R}_5$ ,  
wherein:

30 each of  $R_1$ ,  $R_2$ ,  $R_3$  and  $R_6$  is either  $\text{CH}_3$ ,  $\text{C}_2\text{H}_5$  or  $\text{C}_3\text{H}_7$ ;

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$m = 0 - 2$ ;

$R_4 = \text{CH}_2\text{-CR}_6=\text{CH-CH}_2\text{OH};$

$\text{CH}_2\text{-CR}_6=\text{CH-CHO};$

$\text{CH}_2\text{-CR}_6=\text{CH-COOH};$

5            $\text{CH}_2\text{-CR}_6\text{H-CH}_2\text{-COOH};$

$\text{CH}_2\text{-CR}_6\text{H-CHOH-COOH};$

$\text{CH}_2\text{-CR}_6\text{H-CH}_2\text{-CH}_2\text{OH};$

$\text{CH}_2\text{-CO-CH}_2\text{-COOH};$

$\text{CH}_2\text{-CR}_6\text{H-COOH};$

10            $\text{CHOH}_2\text{-CR}_6\text{H-COOH};$

$\text{CH}_2\text{-CR}_6\text{H-CH}_2\text{-CH}_2\text{OH};$

$\text{CH}_2\text{-CR}_6\text{H-CHO};$

$\text{CH=CR}_6\text{-COOH};$

$\text{CO-CR}_6\text{H-COOH};$

15            $\text{CH}_2\text{-CHOH-CH}_2\text{OH};$

$\text{CH}_2\text{-CO-COOH};$

$\text{CH}_2\text{-COOH};$

$\text{CH}_2\text{-CHO};$

$\text{CH}_2\text{-CH}_2\text{OH};$

20            $\text{CHOH-CH}_2\text{OH};$

$\text{CH}_2\text{-O-CHO};$

$\text{COOH};$  or

$\text{CHO}$  and

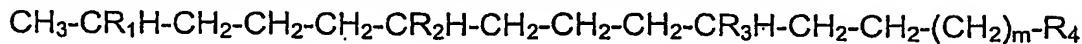
$R_5 = \text{CH}_2\text{-COOH}$  or

25            $\text{COOH},$

or which are a salt, an ester or an amide thereof, in particular chlorophyll, porphyrin, and phospholipid and di- or triacylglycerol esters.

3. A method according to claim 2, characterised in that said product comprises as said PPAR/RXR heterodimer activator or as said

precursor thereof at least one compound selected from the group of compounds which correspond to the following formulas:



wherein:

- 5       $\text{R}_1, \text{R}_2, \text{R}_3$  and  $\text{R}_6 = \text{CH}_3$ ;
- $m = 0$ ; and
- $\text{R}_4 = \text{CH}_2\text{-CR}_6\text{=CH-CH}_2\text{OH}$  (phytol);
- $\text{CH}_2\text{-CR}_6\text{H-CH}_2\text{-COOH}$  (phytanic acid); or
- $\text{CH}_2\text{-CR}_6\text{H-COOH}$  (pristanic acid),
- 10      $\text{COOH}$  (4,8,12-TMTD);

or which are a salt, an ester or an amide thereof, in particular chlorophyll.

4. A method according any one of the claims 1 to 3, characterised in that said PPAR/RXR heterodimer activator is phytanic acid, pristanic acid, TMTD (4,8,12-trimethyltridecanoic acid), a derivative of these acids or a combination thereof, the PPAR/RXR heterodimer activator being preferably phytanic acid and/or pristanic acid.

5. A method according to any one of the claims 1 to 4, characterised in that said product comprises phytol.

6. A method according to any one of the claims 1 to 5, characterised in that the livestock animals are slaughtered to produce said livestock product, in particular to produce skeletal meat, and the livestock animals are made to ingest said product for at least three days during the last week before the slaughtering.

7. A method according to any one of the claims 1 to 6, characterised in that the livestock animals are non-ruminant mammals or poultry, said product being given to the livestock animals so that a level of said PPAR/RXR heterodimer activator of at least 0.2%, preferably of at least 0.5% and more preferably of at least 1.0% of total FAME fatty acids (comprising a linear chain of at least 12 carbon atoms) is achieved in

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said livestock product, in particular in skeletal meat of the livestock animals, the non-ruminant mammals being preferably non-rodents.

8. A method according to claim 7, characterised in that said livestock animals are poultry and said livestock products eggs, said product being given to the livestock animals so that a level of said PPAR/RXR heterodimer activator of at least 1%, preferably of at least 3% and more preferably of at least 5% of total FAME fatty acid is achieved in egg yolk of said eggs.

9. A method according to any one of the claims 1 to 6, characterised in that the livestock animals are ruminants, said product being given to the livestock animals so that a level of said PPAR/RXR heterodimer activator of at least 0.7%, preferably of at least 0.9% and more preferably of at least 1.0% of total FAME fatty acid is achieved in skeletal meat of the livestock animals.

10. A method according to any one of the claims 1 to 6, characterised in that the livestock animals are ruminants, said product being given to the livestock animals so that a level of said PPAR/RXR heterodimer activator of at least 0.75%, preferably of at least 1.0% and more preferably of at least 1.5% of total FAME fatty acids is achieved in milk of the livestock animals.

11. A method according to claim 9 or 10, characterised in that said product comprises chlorophyll in a concentration of at least 0.25% by dry weight, preferably of at least 0.50% by dry weight and more preferably of at least 0.75% by dry weight.

12. A method according to any one of the claims 1 to 6, characterised in that the livestock animals are aquatic animals used to produce said livestock product in aquaculture, said product being given to the livestock animals so that a level of said PPAR/RXR heterodimer activator of at least 0.7%, preferably of at least 0.9% and more preferably

of at least 1.0% of total long chain fatty acids is achieved in said livestock product.

13. A method according to any one of the claims 1 to 12, characterised in that said product is given at least once a day during said period of at least three days, said product being preferably given with the feed of the livestock animals.

5 14. A method according to any one of the claims 1 to 13, characterised in that said predetermined amount of said product contains at least  $25 \times F$  meq., preferably at least  $35 \times F$  meq., more preferably at 10 least  $50 \times F$  meq., and most preferably at least  $65 \times F$  meq of said PPAR/RXR heterodimer activator and/or precursor thereof.

15 15. A method according to any one of the claims 1 to 14, characterised in that said predetermined amount of said product contains less than  $175 \times F$  meq., and preferably less than  $125 \times F$  meq of said PPAR/RXR heterodimer activator and/or precursor thereof.

20 16. A method according to any one of the claims 1 to 15, characterised in that for an initial trial period, during which the livestock animals are made to ingest said product, a parameter influenced by the ingestion of said product in at least a number of the individual livestock animals is determined and, after the initial trial period, the livestock animals are split up into at least two groups based on a difference in effect of said product on said parameter, the parameter which is determined being preferably the gain of weight and/or the feed intake of the individual livestock animals.

25 17. A method to supplement the human diet with a PPAR/RXR heterodimer activator, in which method livestock animals, used in agri- or aquaculture for producing a livestock product for human consumption, are made to ingest at least one product comprising said PPAR/RXR heterodimer activator and/or a precursor thereof which is 30 metabolised by the livestock animals into said PPAR/RXR heterodimer

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activator, over such a period of time and in such an amount that the PPAR/RXR heterodimer activator is accumulated in the livestock animal so that an increased PPAR/RXR heterodimer activator level is achieved in the livestock product, characterised in that said PPAR/RXR heterodimer activator is phytanic acid, a metabolite of phytanic acid, a derivative of phytanic acid or of said metabolite, or a combination thereof and, in order to accumulate the PPAR/RXR heterodimer activator in the livestock animal, a predetermined amount of said product is given to the livestock animals over at least one period of at least three days, during which the livestock animals ingest a total amount of  $F$  kg feed dry weight, which predetermined amount of said product contains at least  $5 \times F$  meq, preferably at least  $10 \times F$  meq, and more preferably at least  $15 \times F$  meq of said PPAR/RXR heterodimer activator and/or precursor thereof.

18. A method for improving the quality of carcass and meat of livestock animals, in particular of pigs, characterised in that the livestock animals are made to ingest at least one product which comprises a PPAR/RXR heterodimer activator selected from the group consisting of phytanic acid, metabolites of phytanic acid, and derivatives of phytanic acid and of said metabolite, and/or a precursor thereof which is metabolised by the livestock animals into said PPAR/RXR heterodimer activator, and, in order to achieve an improved skeletal meat quality, a predetermined amount of said product is given to the livestock animals over at least one period of at least three days, during which the livestock animals ingest a total amount of  $F$  kg feed dry weight, which predetermined amount of said product contains at least  $5 \times F$  meq, preferably at least  $10 \times F$  meq, and more preferably at least  $15 \times F$  meq of said PPAR/RXR heterodimer activator and/or precursor thereof.

19. A method according to claim 18, characterised in that said product comprises phytol.

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20. A livestock product for human consumption obtainable by a method according to any one of the claims 1 to 16, characterised in that the livestock product has an increased level of at least one PPAR/RXR heterodimer activator selected from the group consisting of  
5 phytanic acid, metabolites of phytanic acid, and derivatives of phytanic acid and of said metabolites.

21. A livestock product according to claim 20, characterised in that the livestock product are poultry eggs comprising egg yolk having a level of said PPAR/RXR heterodimer activator of at least 1%,  
10 preferably of at least 3% and more preferably of at least 5% of total FAME fatty acids.

22. A livestock product according to claim 20, characterised in that the livestock product is skeletal meat of non-ruminant mammals or poultry having a level of said PPAR/RXR heterodimer activator of at least  
15 0.2%, preferably of at least 0.5% and more preferably of at least 1.0% of total long chain fatty acids

23. A livestock product according to claim 20, characterised in that the livestock product is skeletal meat of ruminants having a level of said PPAR/RXR heterodimer activator of at least 0.7%, preferably of at  
20 least 0.9% and more preferably of at least 1.0% of total long chain fatty acids.

24. A livestock product according to claim 20, characterised in that the livestock product is milk of ruminants having a level of said PPAR/RXR heterodimer activator of at least 0.75%, preferably of at least  
25 01.0% and more preferably of at least 1.5% of total long chain fatty acids.

25. A feed for livestock animals for use in a method according to any one of the claims 1 to 19, characterised in that it comprises a PPAR/RXR heterodimer activator selected from the group consisting of phytanic acid, metabolites of phytanic acid, and derivatives  
30 of phytanic acid and of said metabolite, and/or a precursor thereof which

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is metabolised by the livestock animals into said PPAR/RXR heterodimer activator, the feed being composed to contain at least 5 meq/kg feed dry weight, preferably at least 10 meq/kg feed dry weight, and more preferably at least 15 meq/kg feed dry weight of said PPAR/RXR heterodimer activator and/or precursor thereof.

26. A feed according to claim 25, characterised in that it contains at least 5 meq/kg feed dry weight, preferably at least 10 meq/kg feed dry weight, and more preferably at least 15 meq/kg feed dry weight of phytol.

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"Livestock products with an increased PPAR/RXR heterodimer activator level"

In the non-therapeutic method livestock animals, used in agri- or aquaculture for producing livestock products, are made to ingest at least one product comprising a PPAR/RXR heterodimer activator and/or a precursor thereof over such a period of time and in such an amount that

5 the PPAR/RXR heterodimer activator is accumulated in the livestock animal. In this way, livestock products such as meat, milk and eggs having an increased PPAR/RXR heterodimer activator level can be obtained. The PPAR/RXR heterodimer activator is phytanic acid, a metabolite of phytanic acid, a derivative of phytanic acid or of said

10 metabolite, or a combination thereof. In order to accumulate the PPAR/RXR heterodimer activator in the livestock animal, a predetermined minimum amount of said product, in particular of phytol, is given to the livestock animals over at least one period of at least three days.

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